

REMARKS

Claims 1-18 are of record pending in this case and stand rejected. Claims 5, 13, 14 and 17 are hereby amended, and no claims are currently added or canceled. Accordingly, claims 1-18 remain pending in the application. Reexamination and reconsideration of claims 1-18 are respectfully requested.

Note, no new matter is believed to be added by any of the amendments hereof or herein. Moreover, any matter cancelled or otherwise no longer in the present claims due to amendment, cancellation or otherwise is intended to be so cancelled or otherwise outside the present scope without prejudice to potential pursuit through continuation or otherwise.

Priority

Applicants note the comments on priority as set forth in the paragraph for cross-references to related applications. Applicants hereby amend that paragraph to remove the language found objectionable. Applicants thus submit that this objection has been obviated and/or traversed and can thus be withdrawn. Action to this end is respectfully requested.

Information Disclosure Statement

Applicants note the comments on reference numbers 37 and 59 of the Information Disclosure Statement (IDS) of January 25, 2007; and in response herewith file corrections therefor. Applicants thus submit that these objections have been obviated and/or traversed and can be withdrawn, and consequently, Applicants respectfully request consideration of the documents cited in and by the corrections hereof. Action to these ends is respectfully requested.

As a side note; Applicants' undersigned representative did on this date also find the Boe, et al. reference (numbered 37) on the Private PAIR Image File Wrapper (IFW) for this case. Moreover, Applicants' representative notes that there exist alternative means for correction of particularly minor inadvertent errors in IDS filings, such as the accidental bona fide failure of inclusion of the year. See MPEP 609.05(a), Form Paragraph 6.51: "The information disclosure statement filed on [1] does not fully comply with the requirements of 37 CFR 1.98(b) because: [2]. Since the submission appears to be *bona fide*, applicant is given ONE (1) MONTH from the date of this notice to supply the above-mentioned omissions or corrections in the information disclosure statement." And see the following Examiner Note: "This practice does not apply

where there has been a deliberate omission of some necessary part of an Information Disclosure Statement or where the requirements based on the time of filing the statement, as set forth in 37 CFR 1.97, have not been complied with.”

Drawings

Applicants note the comments on the drawings and hereby provide replacement drawings to cure the objections thereto. Replacement drawings for FIGs. 2-13 are attached. Applicants thus submit that these objections have been obviated and/or traversed and can thus be withdrawn. Action to this end is respectfully requested.

Specification - Informalities

Applicants note the comments on the specification and the purported informalities related to the PCT application numbers not previously provided; particularly as on pages 8, 11, and 16 of the original application. The specification has been amended hereby to correct the informalities. Applicants further note that evidence was requested in the Office Action indicating that the “PCT numbers being amended ... [are] the same PCT[s] which the applicants had contemplating in incorporation by reference.” See footnote 1, page 3 of the Office Action. Applicants note that such evidence is provided in that the titles of these applications are the same in the original text of the current specification as well as in/on each of the corresponding PCT applications presenting the serial numbers hereby amended into this specification. Moreover, Applicants respectfully note that each of these other three PCT applications referred to here share the same inventorship (Jensen, Thomsen and Veltman), ownership (Thomsen Bioscience A/S), filing date (25 February 2005) and priority date (26 February 2004). It is therefore evident that these are companion cases filed simultaneously by the same people and having intended reference one to another. Applicants thus respectfully submit that these objections have been obviated and/or traversed and can thus be withdrawn. Action to this end is respectfully requested.

Claim Rejections 35 U.S.C. § 112

Applicants note the rejections of claims 5, 6, 13, 14, 16 and 17 for a variety of specific alleged informalities. Applicants note that all of these informalities have been addressed by

amendments herein, and thus, respectfully note that all of these rejections have been obviated and/or traversed and can thus be withdrawn. Actions to these ends are respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 1-18 stand rejected under 35 USC §103(a), as purportedly being unpatentably obvious over various uses of Birmingham et al. (U.S. Patent No. 5,989,824; hereinafter “Birmingham”) in view of Mainelis et al. (Reference number 56 from the IDS of January 25, 2007; hereinafter “Mainelis”), firstly, for claims 1, 2 and 17; or over Birmingham in view of Mainelis and further in view of Johns, et al. (Reference number 47 from the IDS of January 25, 2007; hereinafter “Johns”) for claims 3, 4, 7-9, 13-15 and 18; or over Birmingham in view of Mainelis and further in view of Braven, et al. (Reference number 34 from the IDS of January 25, 2007; hereinafter “Braven”) for claims 5, 6, 10-12 and 16. Applicants respectfully note the obviation of and/or respectfully traverse these rejections for at least the reasons discussed below.

As a preliminary matter, Applicants respectfully note, in short, that Applicants agree that Birmingham does not have “first and second [] electrode[s]” to provide an “electric field” and for “exposing [the biological particle] reaction mixture to an alternating electric field”; nor does Birmingham provide for “contacting the collected biological particle with a first liquid reagent”; Applicants’ claim 1, elements a, c, d and e, emphasis added. Birmingham rather uses “ionized discharges” and “gases”; not electrodes, electric fields and liquids. Thus, Birmingham does not therefore teach or suggest the purported corresponding elements of Applicants’ claims and consequently does not provide a proper basis for rejection under section 103, whether on its own or in view of Mainelis, alone or together with either Johns and/or Braven.

On this, a first essential in patent law is that the proper interpretation of an applicant’s claim terms is that they are to be construed in view of their specifications, see Philips v. AWH discussion herein; Phillips v. AWH Corp., 415 F.3d 1303, 1314, 75 USPQ2d 1321, 1327 (Fed. Cir. 2005). Here, Applicants’ independent claim 1 specifically involves, as defined in Applicants’ specification, a liquid reagent, electrodes and an electric field generated by and between the electrodes which have specific meanings which are definitively different than those of the gas and ionized discharges asserted from Birmingham (any possibility for an electric field to be associated with an ionized discharge, notwithstanding; i.e., Birmingham does not disclose

electric field existence, nor use, and doesn't enable either existence or use; and moreover, none such was asserted in the Office Action, by implication or otherwise).

More particularly, the Patent and Trademark Office ("PTO") determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction "in light of the specification as it would be interpreted by one of ordinary skill in the art." *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364[, 70 USPQ2d 1827] (Fed. Cir. 2004). Indeed, the rules of the PTO require that application claims must "conform to the invention as set forth in the remainder of the specification and the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description." 37 CFR 1.75(d)(1). MPEP 2111 is in accord, the claims are to be interpreted by their broadest reasonable interpretation in view of the specification.

Similarly, a reference disclosure is necessarily limited by what is actually taught or suggested thereby; i.e., limited to what is enabled thereby. The disclosure in an asserted reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. *Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research*, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003). See also, *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968) where it is noted for chemistry-type cases that mere naming of a compound in a reference, without more, cannot constitute a description of the compound.

Note, this concept of "undue experimentation" is substantially the same as that used for judging the enablement of an applicant's disclosure; and, on this, MPEP 2164.03 Relationship of Predictability of the Art and the Enablement Requirement is instructive. In particular, there it is noted that:

in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaecck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work.

What this means here is that Applicants' use of the words "liquid"; "electrodes" and "electric field" in Applicants' specification and claims are directed to very discrete and different elements than the gaseous media and ionizing discharge generator as set forth in or suggested by Birmingham. The asserted elements of Birmingham have different meanings from Applicants' claim words and have different functional and characteristic results therefrom as well.

More particularly, these elements provide for different chemistries and physical activities; particularly, in a primary example, to different rupturing processes; i.e., the rupturing process of Birmingham is quite different from the rupturing process of the present application. Birmingham uses gases and an ionizing discharge generator to generate ionized discharges and uses these ionized discharges to rupture the biological particles in a gaseous medium; e.g., "air [] caused to flow adjacent to a member energized with an ionizing potential[;] ... [t]he ionized air []then [being] directed at the cell." Birmingham, col. 2, lines 61-65. Quite distinctly, a biological particle in Applicants' case is put in contact with a first liquid reagent (see step d) of claim 1) and then it is exposed to the alternating electric field (see step e) of claim 1) established between the first and second electrodes (see step c) of claim 1), where it has surprisingly been found that the particle is ruptured more gently than if the ionized discharge process of Birmingham were used. In this regard Applicants have shown that the morphological changes observed in the coat of biological particles may be indicative of a process that more resembles electroporation rather than complete lysis.

Still furthermore, in the last two lines of page 5 of the Office Action it was alleged that Birmingham discloses contacting the collected biological particle with a **liquid agent**. However, this is not correct, and not enabling thereof. Rather, Birmingham does not disclose any liquids during the rupturing process. Instead, Birmingham only discloses gases such as air and argon. Gases do not teach, suggest or enable a "liquid." Certainly, Birmingham uses the word "fluid"; however, he only describes gases such as air and argon, and does not therefore enable movement toward liquid use (as described further below).

Additionally on this issue of liquids and the failure of enablement thereof, Birmingham could not lead the person skilled in the art to the presently claimed subject matter since ionized discharges do not form in liquid; i.e., Birmingham's use of the word "fluid" could only enable use in gases, liquids not being feasible with the ionized discharges thereof, at least not without undue experimentation. Thus, this is not a mere naming of broader subject matter (mere naming fluids when only gases were intended), nor a mere description of subject matter which is

insufficient (mere lacking of description of liquids), nor even is it merely an issue of undue experimentation or relative unpredictability of the art (would liquids predictably work?) nor a mere chemistry issue (inherent unpredictability); rather, this is a situation where the asserted substitution would apparently not, on its face, work. Again from MPEP 2164.03 there is failure of enablement of the reference “especially ... where the statement is, on its face, contrary to generally accepted scientific principles.” Since ionized discharges do not form in liquid, Birmingham could not have enabled use in/with liquids. Disclosure of the species of air in the genus of fluids did not enable the liquid species.

It is therefore clear that the presently-claimed subject matter is non-obvious in view of the prior art of Birmingham. Mainelis, Johns and Braven do not cure these failures of Birmingham (and indeed are not asserted for such purposes), and thus, the present claims are allowable over any of the purported combinations of these references.

Claims 1, 2 and 17

More particularly, claims 1, 2 and 17 stand rejected under 35 USC §103(a), as allegedly being obvious over Birmingham in view of Mainelis.

Mainelis does not cure the lacking of Birmingham in also not disclosing or suggesting a substitution to or change from the Birmingham system toward “a liquid reagent” or “electrodes” with an “electric field” therebetween. There is no motivation to or from either Birmingham or Mainelis to substitute two electrodes and an associated electric field therebetween for an ionizing discharge generator (Birmingham doesn’t suggest that it may have or want a substitute for the ionizing discharge generator, and Mainelis doesn’t suggest adaptation of its electrodes into a system like Birmingham’s). Moreover, there is no suggestion, nor assertion to achieve a liquid reagent mixture by asserted combination of Mainelis with Birmingham. Mainelis is not even asserted for such a purpose. Birmingham fails to enable a liquid, and Mainelis is not asserted to cure this failure. Thus, there is no motivation or suggestion for combination of Birmingham with Mainelis to result in Applicants’ claimed subject matter, as particularly set forth in independent claim 1 as well as all claims dependent therefrom, including dependent claims 2 and 17, and thus, such alleged combination fails to render obvious Applicants’ claims having such. Claims 1, 2 and 17 are thus patentable over Birmingham in view of Mainelis.

Applicants moreover respectfully submit that Applicants' developments would indeed NOT be obvious to one skilled in the art for the following reasons. "[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." In re Kahn, 441 F. 3d 977, 988 (Fed. Cir. 2006). The law of obviousness requires that there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. KSR International Co. v. Teleflex Inc., 550 U.S. ___, ___, 82 USPQ2d 1385 (2007) and see, e.g., MPEP 2143, inter alia (note, KSR explicitly retained the teaching, suggestion, motivation, TSM, test); see also In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) (concentrating upon what the prior art actually 'taught', 'expressed', 'conveyed', and/or 'spoke of').

Merely combining known prior art elements is not sufficient to render the claimed invention obvious if the results would not have been predictable to one of ordinary skill in the art. KSR; and see, United States v. Adams, 383 U.S. 39,42-43, 51-52, 148 USPQ 479, 480, 483-84 (1966) (stating that "[d]espite the fact that each of the elements . . . was well known in the prior art, to combine them as did Adams required that a person reasonably skilled in the prior art must ignore the teaching away of the prior art . . ."). "When the prior art teaches away from combining certain known elements, discovery of successful means of combining them is more likely to be nonobvious." KSR v. Teleflex, supra, at 1395.

In this case, Applicants' claimed developments of claim 1 include a particle contacted with a liquid reagent and then subjected to an electric field established by and between two electrodes; however, Mainelis does not suggest substitution in or for any part of Birmingham to achieve this; nor vice versa; Birmingham does not suggest or motivate the elimination of the ionizing discharge generator and substituting something other. If Mainelis is cited merely for its teaching of an electric field and electrodes; there nevertheless remains no suggestion for the liquid reagent.

In either case, the Office Action does not however, demonstrate an appropriate suggestion or motivation to the alleged substitution/combination. There is no mechanism detailed, nor steps provided, nor any other information regarding how such would be accomplished or why one would want to make this particular substitution. Note, generalized motivations regarding the benefits to "civilian populations and troops" inter alia, for achieving end functionalities or

greater efficiencies do not provide the type of particularized motivations necessary for the teaching, suggestion, motivation (TSM) test affirmed in KSR; i.e., the motivation for substitution has to be specific, what element substituted where or why, not merely some generalized motivation toward a greater efficiency overall. Therefore, Mainelis does not provide the motivation for substitution to achieve the combination as defined and claimed by Applicants and that Birmingham lacks, and thus Mainelis does not cure the failures of Birmingham.

In short, this situation is not one of simple substitution, nor is it one of a simple ‘upgrade’. See, cf., KSR, supra at ___, 82 USPQ2d at 1399 (discussing ‘upgrading Asano with a sensor’). Applicants’ presently claimed developments involve a combination, not subject to nor being a simple addition, replacement, mounting or an upgrade from Birmingham.

Indeed, there is no teaching or suggestion of an expectation of success from such an alleged modification of Birmingham with Mainelis. See KSR and MPEP 2143. Birmingham and Mainelis have completely operable systems or methods which expect no modification for their particular type of success. It would be unexpected for any of the foregoing to be made over or modified to generate non-suggested elements within the system or method. There is no suggestion or motivation that any particular element is either absent from or needing substitution from either or both of Birmingham and Mainelis; nor that any particular element could or should be incorporated into or onto the Birmingham device, with no rational basis for suggestion how the electrodes of Mainelis would be used to make the substitution. There is no such expectation, thus, no suggestion or motivation for the asserted modification(s). No reasonable expectation of success comes from any of those references. See, e.g., MPEP 2143.01, 2143.02.

In the instant case, a person of ordinary skill in the art having common sense as described in KSR at the time of the invention would not have reasonably looked to Mainelis to solve a problem not even announced in or by either Birmingham or Mainelis. An artisan having common sense at the time of Applicants’ developments would not even be concerned with the ionizing discharge generator of Birmingham, let alone how such might be replaced using a substitute set of electrodes whether like those in Mainelis or otherwise; let alone from where and in what manner such skilled persons might be directed to use of a liquid reagent. Thus, Applicants respectfully submit that the rejection of claims 1, 2 and 17 on Birmingham and Mainelis falls short.

The rejections of claims 1, 2 and 17 are thus obviated or traversed and can and should be withdrawn. Action to this end is respectfully requested.

Claims 3, 4, 7-9, 13-15 and 18

Similarly, claims 3, 4, 7-9, 13-15 and 18 stand rejected under 35 USC §103(a), as purportedly being obvious over Birmingham in view of Mainelis and further in view of Johns.

And, as was the case for Mainelis, Johns does not cure the initial lackings of Birmingham; and, indeed, it was not even asserted for such purpose. Thus, for the same reasons Mainelis failed to supplement Birmingham; all such reasons being incorporated herein as if fully set forth here, Johns also fails to provide all of the missing elements presented in Applicants' claims and thus Applicants' claims are patentable hereover. There is still no teaching or suggestion of the two electrode electric field nor of a liquid reagent. This rejection can thus be withdrawn.

Moreover, Applicant does hereby challenge and respectfully request art citations for the assertion of official notice for the alleged teaching of miniature PCR with particularly any relevance hereof toward and/or teaching/suggestion or motivation therefrom toward the presently-claimed subject matter. Applicants cite Rule 104 for this purpose.

The rejections of claims 3, 4, 7-9, 13-15 and 18 are thus obviated and/or traversed and can and should be withdrawn. Action to this end is respectfully requested.

Claims 5, 6, 10-12 and 16

Lastly, claims 5, 6, 10-12 and 16 stand rejected under 35 USC §103(a), as purportedly being obvious over Birmingham in view of Mainelis and further in view of Braven.

As was the case for either or both of Mainelis and/or Johns above, Braven also fails to cure the failures of Birmingham to provide an electrode defined electric field and/or a liquid reagent. Moreover, as before, there is no motivation for making any substitution or other change in either Birmingham or Mainelis using Braven. Indeed, as described in detail with regard to Mainelis above; such discussion is incorporated herein as if fully set forth here; any generalized motivation for wanting portable devices for sensitive detection is not sufficient for the teaching/suggestion/motivation test in that such motivation says nothing about the specific alteration or substitution which is suggested to or should be effected in the base apparatus or system. In other words, it is not clear from such a generalized motivation what would/should be changed in the Birmingham system nor how such would be achieved. This is thus an improper

basis for alleging a combination of Braven with either or both Birmingham and/or Mainelis. Applicants' claims thus define thereover.

The rejections of claims 5, 6, 10-12 and 16 are thus obviated and/or traversed and can and should be withdrawn. Action to this end is respectfully requested.

Double Patenting – Obviousness Type

Applicants note the provisional double-patenting rejections of the current claims over the claims of two co-pending applications. Applicants agree that these claims are not identical, but do not agree that they are obvious in view of each other, one way or the other. However, in the interests of speedy prosecution, and not in admission of any obviousness one way or the other, Applicants agree that upon the notation of allowable subject matter, they would file a duly signed Terminal Disclaimer to obviate these rejections. These rejections would thus be subject to and may now properly be withdrawn.

CONCLUSION

Applicants note that all rejections are obviated or traversed and respectfully request that they thus be withdrawn. A timely Notice of Allowance is requested to be issued in this case. Applicants believe that no fees or petitions, other than the extension fee/petition set forth above, and the IDS fee, are due with this filing. However, should any such fees or petitions be required, please consider this a request therefore and authorization to charge Deposit Account No. 02-2093 as necessary.

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Respectfully submitted,

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